Protocol

This trial protocol has been provided by the authors to give readers additional information about their work.

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Remdesivir (RDV; GS-5734)
for the Treatment of Selected Coronavirus (CoV) Infection

Single Patient Protocol
(Patient X-X)

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CONFIDENTIAL

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BACKGROUND

1.1. General Information

Remdesivir (RDV; GS-5734) is a nucleotide prodrug that is intracellularly metabolized into an analog of adenosine triphosphate that inhibits viral RNA polymerases and has broad spectrum activity against members of the filoviruses (eg, Ebola virus [EBOV], Marburg virus [MARV]), coronaviruses (eg, severe acute respiratory syndrome [SARS] coronavirus, Middle East respiratory syndrome [MERS] coronavirus [CoV]), and paramyxoviruses (eg, respiratory syncytial virus [RSV], Nipah virus, and Hendra virus). Remdesivir is being developed by Gilead Sciences, Inc. (Gilead) and is formulated for intravenous (IV) administration.

Provided in this document is a single patient protocol for use of RDV for the treatment of a patient with coronavirus disease-2019 (COVID-19) resulting from infection of SARS-CoV-2.

1.2. Rationale for Use of Remdesivir as a Treatment for COVID-19

The recommendation for using RDV as treatment of COVID-19 is based on the in vitro and in vivo activity of RDV against SARS-CoV-2 and other the human highly pathogenic CoVs, MERS-CoV and SARS-CoV.

Recent results from initial in vitro testing performed at the China CDC in collaboration with Gilead showed that RDV has potent antiviral activity against SARS-CoV-2 in Vero cells (EC_{50} = 0.137 μM; preliminary data). In another study conducted by the Wuhan Institute of Virology, RDV also showed in vitro activity against SARS-CoV-2 in Vero cells (EC_{50} = 0.77 μM){Wang }. Gilead notes that the study from the Wuhan Institute of Virology was conducted externally with drug not supplied by Gilead. Researchers in the US and China are continuing to test RDV against clinical isolates of SARS-CoV-2 using drug supplied by Gilead in multiple relevant cell types that are known to more efficiently metabolize RDV into its active triphosphate form compared with Vero cells.

Remdesivir has acceptable nonclinical tolerability and safety profiles and exhibits in vivo prophylactic and therapeutic efficacy against SARS-CoV and MERS-CoV infection in mice and MERS-CoV infection in rhesus monkeys. In addition, RDV has been shown to be generally safe and tolerable, with a safety database of over 500 individuals who have received RDV to date. Key attributes of the RDV nonclinical and clinical profile supporting its use for emergency treatment of COVID-19 are as follows:

- Initial in vitro testing performed at the China CDC in collaboration with Gilead showed that RDV has potent antiviral activity against SARS-CoV-2 in Vero cells (EC_{50} = 0.137 μM). Remdesivir shows potent in vitro activity against the human pathogenic coronaviruses MERS-CoV and SARS-CoV in multiple relevant human cell types.
- The pharmacokinetic (PK) profile of RDV in nonhuman primates (NHPs) and other relevant animal species indicates high and persistent levels of pharmacologically active nucleoside triphosphate metabolite in peripheral blood mononuclear cells (PBMCs), supporting once daily intravenous (IV) administration as a 30-minute infusion.

- Remdesivir demonstrated prophylactic and therapeutic efficacy in a mouse model of SARS-CoV pathogenesis. Administration of 25 mg/kg RDV subcutaneously twice daily beginning 1 day before or 1 day after SARS-CoV inoculation resulted in significantly reduced lung viral load and improved clinical signs of disease as well as lung function {Sheahan 2017}.
- In a mouse model of MERS-CoV pathogenesis, both prophylactic and therapeutic administration of 25 mg/kg RDV subcutaneously twice daily improved pulmonary function and reduced lung viral loads and severe lung pathology. In contrast, prophylactic lopinavir/ritonavir and interferon beta (LPV/RTV-IFNb) slightly reduced viral loads without impacting other disease parameters. Therapeutic LPV/RTV-IFNb improved pulmonary function but did not reduce virus replication or severe lung pathology {Sheahan 2020}.
- Remdesivir also showed prophylactic and therapeutic efficacy in MERS-CoV-infected rhesus monkeys of Indian origin. Administration of RDV at 10 mg/kg (see RDV Investigator's Brochure [IB]) or 5 mg/kg once daily using IV bolus injection beginning 1 day prior to MERS-CoV inoculation resulted in a significant reduction of clinical scores, clinical signs of respiratory disease, and viral RNA levels compared to vehicle-treated animals. Therapeutic RDV treatment of 5 mg/kg once daily for 7 days using IV bolus injection initiated 12 hours post-inoculation also resulted in reduced clinical signs, reduced virus replication in the lungs, and decreased presence and severity of lung lesions {De Wit 2020}.
- The target organ identified in the repeat-dose toxicology studies was the kidney in both rats and monkeys. Clinical chemistry, urinalysis, and urine biomarkers were early indicators of the reversible microscopic changes observed in the kidneys.
- Remdesivir has a favorable clinical safety profile based on approximately 500 individuals who received RDV primarily as healthy volunteers in Phase 1 studies and individuals with acute EBOV infection.

It is unknown, at present, how the observed efficacy of RDV in animal models of coronavirus infection will translate into clinical efficacy in patients with symptomatic disease.

Reference safety information, an overview of nonclinical experience, an overview of clinical experience, investigator guidance, and physical, chemical, and pharmaceutical information is provided in the RDV IB.

2. DESCRIPTION OF PATIENT'S DISEASE/CONDITION, INCLUDING RECENT MEDICAL HISTORY AND PREVIOUS TREATMENTS

Provided below is information regarding the patient's disease/condition, medical history, and previous treatments.

Patient initials:

DOB:

Sex:

Diagnosis: *[[Provide here or refer to Appendix 1]]*

Current treatment: *[[Provide here or refer to Appendix 1]]*

Current Medication list: *[[Provide here or refer to Appendix 1]]*

Laboratory tests (including Cr clearance, ALT, AST): *[[Provide here or refer to Appendix 1]]*

History and presentation of illness: *[[Provide here or refer to Appendix 1]]*

3. DRUG DESCRIPTION AND DOSAGE

Remdesivir is a single diastereomer monophosphoramidate prodrug of a nucleoside analog GS-441524.

3.1. Special Dosing Considerations

Coronavirus infection can progress to the severe life-threatening stage of disease involving severe pneumonia and acute respiratory distress syndrome. In these cases, treatment with RDV might have only limited, if any, impact on the survival of the infected subjects. In order to maximize its impact on viral replication and the chance of a successful outcome, it is important to initiate patient treatment with RDV as soon as possible following the diagnosis of identified CoV infection. Remdesivir may only be administered in accordance with applicable local regulatory requirements.

3.2. Route of Administration

Intravenous (IV) infusion administered over a 30 to 60 minute period.

3.3. Formulation

3.3.1. Solution Formulation, Remdesivir (GS-5734) Injection

The solution formulation of remdesivir is supplied as a sterile, preservative-free, clear, colorless to yellow, aqueous-based concentrated solution containing 5 mg/mL remdesivir to be diluted into infusion fluids prior to IV administration. It is supplied as a sterile product in a single-use, clear glass vial with sufficient volume to allow withdrawal of 20 mL (100 mg remdesivir). In addition to the active ingredient, the solution formulation of remdesivir contains the following inactive ingredients: water for injection, sulfobutylether β-cyclodextrin sodium (SBECD), and hydrochloric acid and/or sodium hydroxide. Hydrochloric acid and/or sodium hydroxide are used to adjust the formulation to a final pH of 3.0 to 4.0.

3.3.2. Lyophilized Formulation, Remdesivir (GS-5734) for Injection

The lyophilized formulation of remdesivir is a preservative-free, white to off-white or yellow, lyophilized solid containing remdesivir to be reconstituted with sterile water for injection and diluted into IV infusion fluids prior to IV administration. It is supplied as a sterile product in a single-use, clear glass vial. Following reconstitution, each vial contains a 5 mg/mL remdesivir concentrated solution with sufficient volume to allow withdrawal of 20 mL (100 mg of remdesivir). In addition to the active ingredient, the lyophilized formulation of remdesivir contains the following inactive ingredients: water for injection, SBECD, hydrochloric acid, and/or sodium hydroxide. Hydrochloric acid and/or sodium hydroxide are used to adjust the formulation to a final pH of 3.0 to 4.0.

Detailed information regarding study drug administration, reconstitution, and dilution instructions are provided in a pharmacy manual provided to the investigator.

3.4. Dosage for Treatment of Coronavirus Infection

3.4.1. Adult Patient

The proposed regimen for the treatment of established CoV infection, including SARS-CoV, MERS-CoV, and SARS-2-CoV is as follows: single RDV 200 mg IV loading dose on Day 1 of treatment followed by 100 mg IV once-daily maintenance doses on Days 2 - 10. The recommended RDV dosing duration is a total of 10 days.

The proposed dosing regimen is based on clinical safety data in approximately 500 individuals, including healthy volunteers, individuals with acute EBOV infection, individuals exposed to EBOV, as well as Ebola survivors, with supportive data from efficacy studies in MERS-infected rhesus monkeys treated with RDV (Studies PC-399-2037 and PC-399-2038).

In the nonclinical studies, RDV was administered at 10 mg/kg (Study PC-399-2038) or 5 mg/kg (Study PC-399-2037) once daily for 7 days using IV bolus injection beginning either 1 day prior to (10 mg/kg or 5 mg/kg dose) or 12 hours after (5 mg/kg dose only) MERS-CoV inoculation. RDV treatment was efficacious at reducing viral titers in the lung and alleviating clinical disease signs (RDV IB; {De Wit 2020}).

Final results from Studies GS-US-399-1812 and GS-US-399-1954 and preliminary results from Studies GS-US-399-4231 and GS-US-399-5505 indicate that remdesivir is generally safe and well tolerated at a single dose of 3 to 225 mg (Studies GS-US-399-1812 and GS-US-399-4231) and multiple doses of 150 mg once daily for 7 or 14 days (Study GS-US-399-1954) or 200 mg at Day 1 and then 100 mg once daily for 4 or 9 days (GS-US-399-5505).

Transient treatment-emergent elevations in ALT and AST were observed during the studies, none of which were graded in the single-ascending dose study, and all of which were Grade 1 or Grade 2 in the multiple-dose studies. Some ALT and AST elevations were associated with graded PT elevations; however, there were no graded changes in INR. Laboratory results for these subjects indicated no systemic sign of drug reaction. Overall, no other clinically relevant consistent patterns of laboratory abnormalities or changes from baseline in laboratory parameters were noted during the studies. Additional detail is available in the IB.

A total of 174 patients received RDV in the PALM 1 Ebola therapeutics trial. An additional 221 patients received RDV for acute Ebola virus disease under the Monitored Emergency Use for Unregistered Interventions (MEURI) protocol. Other patients who have received RDV include male Ebola survivors, post exposure prophylaxis, as well as compassionate use for other indications. No significant adverse events or laboratory abnormalities were attributed to RDV.

Toxicology studies in cynomolgus monkeys and rats and safety, pharmacokinetic studies in healthy volunteers and safety data from > 500 individuals support the safety of the proposed dose.

3.4.2. Pediatric Patient

A proposed pediatric dose regimen aims to achieve daily therapeutic exposures of RDV comparable to those in adults, while considering the risk:benefit profile for the renally eliminated metabolite, GS-441524, that may accumulate in pediatric patients with immature clearance pathways.

To this end, physiologically-based pharmacokinetic models (SimCYP, v.16) were developed to model adult RDV and GS-441524 exposure and predict pediatric patient exposure based on age-dependent physiologic changes (eg, organ volume/function, blood flow, etc). These simulations do not account for the impact of infection on the pharmacokinetics of GS-5734 and GS-441524 which is currently unknown.

The results of these simulations indicate:

- For pediatric patients with body weight ≥ 40 kg, the adult dosage regimen of one loading dose of RDV 200 mg IV (infused over 30 to 60 min) on Day 1 followed by RDV 100 mg IV (infused over 30 to 60 min) once daily for 9 days will be administered. Use of the adult dose in these pediatric patients is expected to maintain exposures of both RDV and GS-441524 at or below those previously observed to be generally well tolerated in the 14-day multiple dose study in adult healthy volunteers (N=24, Study GS-US-399-1954).

- For pediatric patients with body weight < 40 kg, a body weight-based dosing regimen of one loading dose of RDV 5 mg/kg IV (infused over 30 to 60 min) on Day 1 followed by RDV 2.5 mg/kg IV (infused over 30 to 60 min) once daily for 9 days will be administered. Use of this weight-based regimen is expected to maintain RDV exposure that is comparable to that observed in adults while limiting the exposure of GS-441524 in very young children.

3.4.3. Patients with Renal and/or Hepatic Impairment

There are no specific studies conducted with RDV in patients with renal and/or hepatic impairment. A substantial proportion of patients with acute Ebola virus disease who received treatment with RDV under the PALM and MEURI protocols had moderate to severe liver and renal abnormalities at presentation. No renal or hepatic abnormalities were attributed to RDV. Given the benefit-risk ratio in patients with acute CoV infection, no dose modification is recommended at the present time.

4. DESCRIPTION OF CLINICAL PROCEDURES, LABORATORY TESTS, OR OTHER MONITORING

Described below are clinical procedures, laboratory tests, and other monitoring necessary to evaluate the effects of the drug and minimize its risks.

4.1. Clinical Procedures

During treatment with RDV, the patient will be admitted as an inpatient at a facility staffed and maintained by the requesting physician. A peripheral IV line or other venous catheter will be maintained. Fluid resuscitation will be available if necessary in the event of signs of renal failure or hypotension. Fever will be treated with acetaminophen (up to maximum allowable daily dose) and antibiotics as indicated. It is recommended that use of nonsteroidal anti-inflammatory medications and other nephrotoxic agents be avoided, if possible.

4.2. Laboratory Tests

The following laboratory tests will be performed daily during RDV therapy: serum chemistries—including electrolytes, renal function tests (creatinine, CrCL, BUN), liver function tests (including ALT, AST, total bilirubin, and alkaline phosphatase), hematology (complete blood count and prothrombin time) and urinalysis. CoV PCR, if available, should be performed at regular intervals to monitor response to RDV therapy and to continually weigh the risks and benefits to the patient. Other lab and clinical parameters will be checked at the discretion of the physician.

All available laboratory and clinical results will be shared daily with the drug manufacturer (Gilead) via either the provided Clinical Update Form or electronically through eCRF, and the action plan for adverse events and abnormal laboratory results will be discussed with Gilead.

4.3. Other Monitoring

Physical examination and vital signs will be monitored at least once daily.

Concomitant administration of other investigational agents for COVID-19 is not permitted while receiving remdesivir.

Gilead should be notified prior to study drug discontinuation when medically feasible. Remdesivir should be permanently discontinued in the following conditions:

- Development of ALT levels $\geq$ 5 times the upper limit of normal
- Estimated creatine clearance < 30 mL/min based on the Cockcroft-Gault formula
- For clinical queries please contact Gilead: MM-COVID19@gilead.com

5. BENEFIT-RISK ASSESSMENT

There are currently no investigational agents with demonstrated clinical efficacy or approved treatments for acute severe CoV infection. The timely assessment of a safe and effective antiviral agent that works by directly and selectively blocking the virus replication and is broadly efficacious against human pathogenic CoVs would address a serious unmet medical need, benefiting both infected individuals and the affected community.

The pharmacokinetics of a single 5 mg/kg dose in healthy rhesus monkeys and a single dose of 75 mg in healthy adult human volunteers, both administered as 30-min IV infusion using the lyophilized formulation of RDV, demonstrated similar systemic plasma exposures of RDV. Additionally, the intracellular exposures of the active nucleoside triphosphate metabolite GS-443902 observed in rhesus monkey PBMCs were in the range of those observed in human PBMCs. Based on the dose-proportional pharmacokinetics observed in both species, drug exposure from the loading dose of 10 mg/kg in rhesus monkeys is similar to the expected drug exposure from the loading dose of 200 mg in humans. Toxicology studies in cynomolgus monkeys and rats and safety and pharmacokinetic studies in healthy volunteers support the safety of the proposed dose. Overall, RDV has a favorable pharmacokinetic and safety profile that supports evaluation of a 200 mg loading and a 100 mg daily dose that has potential to be efficacious in adult patients infected with coronavirus.

Transient treatment-emergent elevations in ALT and AST (Grade ≤ 2), have been observed after multiple daily RDV administration in Studies GS-US-399-1954 and GS-US-399-5505. To date in human studies, no SAEs have occurred in healthy individuals who have received at least 1 dose of RDV. Remdesivir has been tested in healthy volunteers as a single ascending dose over a dose range of 3 to 225 mg and in a multi-dose study of 150mg for up to 14 days and at 200 mg loading dose followed by 100mg for a total of 10 days. The potential changes in transaminases in CoV-infected patients treated with RDV can be readily monitored by standard clinical chemistry laboratory tests.

In nonclinical animal studies, toxicity findings were consistent with dose-dependent and reversible kidney injury and dysfunction. The clinical significance of the nephrotoxicity noted in animal species is unknown. The etiology of reversible kidney injury observed in rats is consistent with the ability of rat renal organic anion transporters (OATs), but not human OATs, to efficiently interact with blood metabolites of remdesivir, particularly GS-704277. This effect may lead to proportionally higher intracellular accumulation of drug metabolites in renal rat tubules, leading to kidney injury.

The 200 mg loading dose with 8 g of sulfobutylether β-cyclodextrin sodium (SBECD) on day 1 will be followed by 100 mg of RDV each day for 4 or 9 days with 4 g of SBECD, which is within the range of daily SBECD administration considered safe in humans. A total of 250 mg/kg/day of SBECD is considered safe by European Medicines Agency and is therefore safe for all adults with weight over 32 kg. The 100 mg dose prepared in 0.9% saline will be hypertonic relative to human serum osmolality but approaches the normal physiological osmolar range for humans. Renal function can be readily monitored by standard clinical chemistry tests.

The PALM 1 Ebola therapeutics study was a randomized, controlled, open label, trial comparing the ZMapp control to three putative Ebola therapeutics— RDV, REGN-EB3, and mAb114—for reductions in 28-day mortality in patients with acute EVD.{Mulangu 2019}. ZMapp, REGN-EB3, and mAb114 are monoclonal-based therapies. One patient receiving RDV had hypotension during administration of the loading dose followed by cardiac arrest. This serious adverse event (SAE) was deemed possibly related to RDV by the pharmacovigilance committee. An additional 221 patients received RDV for acute Ebola virus disease under the MEURI protocol.

PREVAIL IV was double-blind, 1:1 randomized, two-phase, placebo-controlled, Phase II Trial of RDV dosed at100 mg daily for 5 days designed to assess the antiviral activity, longer-term clearance of seminal EBOV RNA, and safety in Liberian and Guinean men with persistent EBOV RNA in semen. The study enrolled 38 of a planned 60-120 participants, of which 20 received RDV. There were no SAEs. The study allowed for blinded dose reductions for transaminase elevations; there was 1 individual dose reduction in the RDV arm and 5 in the placebo arm.

The first confirmed case of COVID-19 in the US was a 35-year-old previously healthy man who returned from Wuhan, China and was admitted to Providence Regional Medical Center in Washington state with a 4-day history of cough and subjective fever {Holshue 2020}. The patient tested positive for SARS-CoV-2 on illness day 4, progressed to pneumonia on illness day 9 and developed atypical pneumonia on illness day 10. The patient was treated with remdesivir, and no AEs were observed in association with its administration. As of illness day 15, the patient was afebrile and all symptoms were resolved, except for the cough, which was resolving.

There are currently no data available on the interaction of RDV and other investigational agents. Administering RDV concurrent with other investigational anti-CoV agents may lead to antagonism, synergy, or have no effect.

Overall, the toxicology studies in cynomolgus monkeys and rats, and safety and pharmacokinetic studies in healthy human volunteers and patients with EBOV infection support the safety of the RDV proposed dose. In consideration of the information included in this protocol, the overall risks to patients are outweighed by the potential benefits of RDV experimental therapy for the treatment of potentially coronavirus infection.

In conclusion, RDV has a favorable safety profile that supports evaluation of the proposed dosing regimen with a potential to be efficacious in patients infected with CoV.

6. REFERENCES

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Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and Chloroquine Effectively Inhibit the Recently Emerged Novel Coronavirus (2019-nCoV) In Vitro. Cell research 2020:1-3.

7. APPENDICES

Appendix 1 **Clinical Baseline Assessment Form**

Appendix 2 **Clinical Update Form**

Appendix 3 **Post-treatment Follow-Up Form (7 day and 14 day)**

Clinical Baseline Assessment Form
This form is ONLY to be completed via email if EDC (https://www.imedidata.com) is unavailable at your site and you are prompted to do so by Gilead Clinical Operations. Please provide as much of the information below as possible and submit to remdesivir_CDM@gilead.com

Patient ID

Institution Name:_____

Physician Name: _____

Patient Initials (XXX): __ __ __

Sex at Birth: [ ] Male [ ] Female

Date of Birth (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Pregnant: [ ] Yes [ ] No [ ] Unknown [ ] NA

Breastfeeding: [ ] Yes [ ] No [ ] Unknown [ ] NA

COVID-19 Disease Status

Current date (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Currently hospitalized? [ ] Yes [ ] No

Currently in Intensive Care Unit (ICU) or Critical Care Unit (CCU)?? [ ] Yes [ ] No

First hospital admission date for COVID-19 (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

COVID-19 Symptom onset date (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Was SARS-CoV-2 confirmed by PCR test? [ ] Yes [ ] No

Radiographic evidence of pulmonary infiltrates? [ ] Yes [ ] No

If Yes, please describe:

Current Vital Signs

Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Collection Time (00:00 – 23:59): __ __ : __ __

Max Body Temperature in Last 24 hours	_____	Units: [ ] Celsius [ ] Fahrenheit	Location: [ ] Armpit [ ] Ear [ ] Oral [ ] Rectum
Resting Respiratory Rate (breaths/min)	_____		
Resting Heart Rate (beats/min)	_____		
SBP (mmHg)	_____		

DBP (mmHg)	_____
Level of Consciousness	[ ] Alert [ ] Arousable only to Voice or Pain [ ] Unresponsive

Clinical Support, Limitations, and Infection Control

Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Collection Time (00:00 – 23:59): __ __ : __ __	
Currently on room air?	[ ] Yes [ ] No If Yes, please enter oxygen saturation (SpO_2, %):_____
Currently requiring low-flow oxygen therapy (via low-flow nasal cannula or prongs, simple face mask, etc)?	[ ] Yes [ ] No If Yes, then indicate supplemental oxygen amount: ____(L / min) or _____% FiO_2 If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Currently requiring high-flow oxygen (via e.g., high-flow nasal cannula)?	[ ] Yes [ ] No If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Currently requiring non-invasive positive pressure ventilation (via BIPAP, CPAP, etc)?	[ ] Yes [ ] No If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Currently requiring mechanical ventilation (via endotracheal tube, tracheostomy tube, etc)?	[ ] Yes [ ] No If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Currently requiring ECMO support?	[ ] Yes [ ] No If Yes, please indicate type: [ ] V-V [ ] V-A If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Ongoing medical care preventing hospital discharge (COVID-19 related or other medical condition)?	[ ] Yes [ ] No
Limitations of physical activity (self assessed)?	[ ] Yes [ ] No
Requiring vasopressor or inotropic support?	[ ] Yes [ ] No

Other information on clinical course, exposure history, current clinical status

Past Medical History

Medical History Condition	Start Date	Stop Date or indicate as Ongoing

Medications taken in last 48 hours

Include other antiviral medications (e.g., lopinavir/ritonavir, interferon, oseltamivir, etc)

Medication Name	Indication	Dose	Route	Start Date	Stop Date or indicate as Ongoing

Most Recent Laboratory Measures[a]

Chemistry Specimen Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Chemistry Specimen Collection Time (00:00 – 23:59): __ __ : __ __		
Lab Name	Result	Units
Alanine aminotransferase (ALT)		
Alkaline Phosphatase		
Aspartate Aminotransferase (AST)		
Bicarbonate		
Blood Urea Nitrogen (BUN)		
Chloride		
Creatinine		
Creatinine Clearance – Cockcroft-Gault[b]		
Creatinine Clearance – eGFR[b]		

Creatinine Clearance – CKD-EPI[b]		
Potassium		
Sodium		
Total Bilirubin		
Hematology Specimen Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Hematology Specimen Collection Time (00:00 – 23:59: __ __ : __ ____ __		
Lab Name	Result	Units
White Blood Cells		
Hemoglobin		
Hematocrit		
Platelets		
Neutrophils		
Lymphocytes		
Eosinophils		
Coagulation Specimen Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Coagulation Specimen Collection Time (00:00 – 23:59: __ __ : __ __		
Lab Name	Result	Units
Prothrombin Time		
International Normalized Ratio		
Activated Partial Thromboplastin Time		

SARS-CoV-2 PCR Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ SARS-CoV-2 PCR Specimen Collection Time (00:00 – 23:59: __ __ : __ __			
Lab Name	Specimen Source (nasopharynx, oropharynx, BAL, sputum, stool, blood)	Result	Units
SARS-CoV-2 PCR - qualitative			
SARS-CoV-2 PCR - quantitative			

[a] Representative template for lab reporting. Can alternatively forward lab report (with personally identifying information removed)

[b] Need enter only one Creatinine Clearance measure

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Single Patient Protocol

Clinical Update Form
This form is ONLY to be completed via email if EDC (https://www.imedidata.com) is unavailable at your site and you are prompted to do so by Gilead Clinical Operations. Please provide as much of the information below as possible and submit to remdesivir_CDM@gilead.com

Patient ID

Institution Name:_____

Physician Name: _____

Patient Initials (XXX): __ __ __

Sex at Birth: [ ] Male [ ] Female

Date of Birth (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Clinical Summary

Date (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Currently hospitalized? [ ] Yes [ ] No If No, please enter date of hospital discharge:

Date (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Currently in Intensive Care Unit (ICU) or Critical Care Unit (CCU)? [ ] Yes [ ] No

Remdesivir Dosing

Number of Remdesivir doses received (total course): ___

Most Recent Remdesivir Dose Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __

Most Recent Remdesivir Dose Start Time (00:00 – 23:59): __ __ : __ __

Final Dose of Remdesivir regimen? [ ] Yes [ ] No

Adverse Events:
Please list any new adverse events/serious adverse events not previously reported, including cause of death:

Adverse Event	Serious* (indicate Yes or No) ***If Yes, please complete a Solicited Program Adverse Event/Special Situation Report Form and submit to Safety_FC@gilead.com***	Start Date	End Date or indicate as Ongoing	Related to Remdesivir (indicate as Related or Not Related)	Action Taken with Remdesivir (indicated as Dose Not Changed, Drug Interrupted, or Drug Withdrawn)

*As outlined in Prescriber's Agreement (Attachment A)

Current Vital Signs

Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Collection Time (00:00 – 23:59): __ __ : __ __			
Max Body Temperature in Last 24 hours	_____	Units: [ ] Celsius [ ] Fahrenheit	Location: [ ] Armpit [ ] Ear [ ] Oral [ ] Rectum
Resting Respiratory Rate (breaths/min)	_____		
Resting Heart Rate (beats/min)	_____		
SBP (mmHg)	_____		
DBP (mmHg)	_____		
Level of Consciousness	[ ] Alert [ ] Arousable only to Voice or Pain	[ ] Unresponsive	

Clinical Support, Limitations, and Infection Control

Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Collection Time (00:00 – 23:59): __ __ : __ __	
Currently on room air?	[ ] Yes [ ] No If Yes, please enter oxygen saturation (SpO_2, %):_____
Currently requiring low-flow oxygen therapy (via low-flow nasal cannula or prongs, simple face mask, etc)?	[ ] Yes [ ] No If yes, then indicate supplemental oxygen amount: ____(L / min) or _____% FiO_2
Currently requiring high-flow oxygen (via e.g., high-flow nasal cannula)?	[ ] Yes [ ] No
Currently requiring non-invasive positive pressure ventilation (via BIPAP, CPAP, etc)?	[ ] Yes [ ] No
Currently requiring mechanical ventilation (via endotracheal tube, tracheostomy tube, etc)?	[ ] Yes [ ] No
Currently requiring ECMO support?	[ ] Yes [ ] No If Yes, please indicate: [ ] V-V [ ] V-A

Ongoing medical care preventing hospital discharge (COVID-19 related or other medical condition)?	[ ] Yes	[ ] No
Limitations of physical activity (self assessed)?	[ ] Yes	[ ] No
Requiring vasopressor or inotropic support?	[ ] Yes	[ ] No

Radiographic results in last 24 hours (e.g., X-ray, CT scan, etc.)? [ ] No [ ] Yes

If Yes, please describe:

Other information on clinical course, exposure history, current clinical status

Current Laboratory Measures[a]

Chemistry Specimen Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Chemistry Specimen Collection Time (00:00 – 23:59): __ __ : __ __

Lab Name	Result	Units
Alanine aminotransferase (ALT)		
Alkaline Phosphatase		
Aspartate Aminotransferase (AST)		
Bicarbonate		
Blood Urea Nitrogen (BUN)		
Chloride		
Creatinine		
Creatinine Clearance – Cockcroft-Gault[b]		
Creatinine Clearance – eGFR[b]		
Creatinine Clearance – CKD-EPI[b]		
Potassium		
Sodium		

Total Bilirubin		
Hematology Specimen Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Hematology Specimen Collection Time (00:00 – 23:59: __ __ : __ ____ __		
Lab Name	Result	Units
White Blood Cells		
Hemoglobin		
Hematocrit		
Platelets		
Neutrophils		
Lymphocytes		
Eosinophils		
Coagulation Specimen Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Coagulation Specimen Collection Time (00:00 – 23:59: __ __ : __ __		
Lab Name	Result	Units
Prothrombin Time		
International Normalized Ratio		
Activated Partial Thromboplastin Time		

SARS-CoV-2 PCR Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ SARS-CoV-2 PCR Specimen Collection Time (00:00 – 23:59: __ __ : __ __			
Lab Name	Specimen Source (nasopharynx, oropharynx, BAL, sputum, stool, blood, etc.)	Result	Units
SARS-CoV-2 PCR - qualitative			
SARS-CoV-2 PCR - quantitative			

[a] Representative template for lab reporting. Can alternatively forward lab report (with personally identifying information removed)

[b] Need enter only one Creatinine Clearance measure

Concomitant Medications

Drug Name	Indication	Dose	Route	Start Date	Stop Date or indicate as Ongoing

Remdesivir (RDV; GS-5734) for the Treatment of Selected Coronavirus (CoV) Infection
Single Patient Protocol

Post-treatment Follow-Up Form (7 day and 14 day)

Please submit the Clinical Follow-Up Form (7 day and 14 day) to Gilead Data Management (remdesivir_cdm@gilead.commailto:) or enter data directly into EDC (https://www.imedidata.com). Only one method is required: EDC or email.

Patient ID

Institution Name:_____ Physician Name: _____

Patient Initials (XXX): __ __ __ Sex at Birth: [ ] Male [ ] Female

Date of Birth (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Course of Follow-up

Current Date (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Date of last Remdesivir Dose: (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Patient Status

Vital Status: [ ] Alive [ ] Deceased [ ] Unknown

Currently hospitalized? [ ] Yes [ ] No [ ] Unknown If No, please enter date of hospital discharge:

Date (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Currently in Intensive Care Unit (ICU) or Critical Care Unit (CCU)? [ ] Yes [ ] No [ ] Unknown

Adverse Events:
Please list any new adverse events/serious adverse events not previously reported, including cause of death if applicable:

Adverse Event	Serious* (indicate Yes or No) ***If Yes, please complete a Solicited Program Adverse Event/Special Situation Report Form and submit to Safety_FC@gilead.com***	Start Date	End Date or indicate as Ongoing	Related to Remdesivir (indicate as Related or Not Related)	Action Taken with Remdesivir (indicated as Dose Not Changed, Drug Interrupted, or Drug Withdrawn)

*As outlined in Prescriber's Agreement (Attachment A)

Clinical Support, Limitations, and Infection Control

Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Collection Time (00:00 – 23:59): __ __ : __ __	
Currently on room air?	[ ] Yes [ ] No If Yes, please enter oxygen saturation (SpO_2, %):_____
Currently requiring low-flow oxygen therapy (via low-flow nasal cannula or prongs, simple face mask, etc)?	[ ] Yes [ ] No If yes, then indicate supplemental oxygen amount: ____(L / min) or _____% FiO_2
Currently requiring high-flow oxygen (via e.g., high-flow nasal cannula)?	[ ] Yes [ ] No
Currently requiring non-invasive positive pressure ventilation (via BIPAP, CPAP, etc)?	[ ] Yes [ ] No
Currently requiring mechanical ventilation (via endotracheal tube, tracheostomy tube, etc)?	[ ] Yes [ ] No
Currently requiring ECMO support?	[ ] Yes [ ] No